

Refine Search

Search Results -

Term	Documents
(8 NOT 5).PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD.	84
(L8 NOT L5).PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD.	84

Database: US Pre-Grant Publication Full-Text Database
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 US OCR Full-Text Database
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 JPO Abstracts Database
 Derwent World Patents Index
 IBM Technical Disclosure Bulletins

Search:

L9	<input type="button" value="Refine Search"/>
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Search History

DATE: Tuesday, April 04, 2006 [Printable Copy](#) [Create Case](#)

<u>Set Name</u>	<u>Query</u>	<u>Hit Count</u>	<u>Set Name</u>
<u>side by side</u>			<u>result set</u>
<i>DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; THES=ASSIGNEE; PLUR=YES; OP=AND</i>			
<u>L9</u>	L8 not L5	84	<u>L9</u>
<u>L8</u>	L7 and (pulmonary or lung or intranasal)	95	<u>L8</u>
<u>L7</u>	L6 and L4	142	<u>L7</u>
<u>L6</u>	(Factor adj VIII) and (Hemophilia adj B)	458	<u>L6</u>
<u>L5</u>	L4 same (pulmonary or lung or intranasal)	59	<u>L5</u>
<u>L4</u>	(Factor adj VIII) same (vector)	997	<u>L4</u>
<u>L3</u>	L2 and (Factor adj VIII)	2	<u>L3</u>
<u>L2</u>	Cheng-Seng.in.	4	<u>L2</u>
<u>L1</u>	Li-Chester.in.	2	<u>L1</u>

END OF SEARCH HISTORY

 **PALM INTRANET**

Day : Tuesday
Date: 4/4/2006
Time: 15:02:23

Inventor Name Search

Enter the first few letters of the Inventor's Last Name.
Additionally, enter the first few letters of the Inventor's First name.

Last Name**First Name**

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 PALM INTRANET

Day : Tuesday
Date: 4/4/2006
Time: 15:02:23

Inventor Name Search

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Last Name**First Name**

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PALM INTRANET

Day : Tuesday
Date: 4/4/2006
Time: 15:02:23

Inventor Name Search

Enter the first few letters of the Inventor's Last Name.
Additionally, enter the first few letters of the Inventor's First name.

Last Name Li**First Name** Chester

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Dialog level 05.10.03D
Last logoff: 31mar06 13:17:13
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*** ANNOUNCEMENTS ***

NEW FILES RELEASED

***Regulatory Affairs Journals (File 183)
***Index Chemicus (File 302)
***Inspec (File 202)

RELOADS COMPLETED

*** MEDLINE has been reloaded with the 2006 MeSH (Files 154 & 155)
*** The 2005 reload of the CLAIMS files (Files 340, 341, 942)
is now available online.

RESUMED UPDATING

***EDGARPLUS (TM)-Williams Act Filings (File 773)
***EDGARPLUS (TM)-Prospectuses (File 774)
***EDGARPLUS (TM)-Registration Statements (File 775)
***EDGARPLUS (TM)-6K, 8K, and 10C Filings (File 776)
***EDGARPLUS (TM)-10-K & 20F Filings (File 778)
***EDGARPLUS (TM)-10-Q Filings (File 779)
***EDGARPLUS (TM)-Proxy Statements (File 780)

Chemical Structure Searching now available in Prous Science Drug Data Report (F452),
IMS R&D Focus (F445/955), Pharmaprojects (F128/928), Beilstein
Facts (F390), Derwent Chemistry Resource (F355) and Index Chemicus
(File 302).

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KWIC is set to 50.

HIGHLIGHT set on as ''

* * *

File 1:ERIC 1966-2006/Feb
(c) format only 2006 Dialog

Set Items Description

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Cost is in DialUnits
?

B 155, 5, 73
04apr06 15:28:03 User259876 Session D859.1
\$0.82 0.233 DialUnits File1
\$0.82 Estimated cost File1
\$0.05 INTERNET
\$0.87 Estimated cost this search
\$0.87 Estimated total session cost 0.233 DialUnits

SYSTEM:OS - DIALOG OneSearch

File 155: MEDLINE(R) 1951-2006/Apr 04
(c) format only 2006 Dialog

*File 155: Medline has been reloaded. Some accession numbers
have changed.

File 5:Biosis Previews(R) 1969-2006/Mar W4

(c) 2006 BIOSIS
File 73:EMBASE 1974-2006/Apr 04
(c) 2006 Elsevier Science B.V.

Set Items Description
--- ----- -----

?

S (HEMOPHILA (W) B) (S) (THERAPY OR TREATMENT)
84 HEMOPHILA
2238482 B
5811769 THERAPY
5097651 TREATMENT
S1 2 (HEMOPHILA (W) B) (S) (THERAPY OR TREATMENT)

?

RD

S2 2 RD (unique items)

?

T S2/3,K/ALL

2/3,K/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2006 BIOSIS. All rts. reserv.

0007878455 BIOSIS NO.: 199192124226

EXPRESSION OF HUMAN FACTOR IX IN RAT CAPILLARY ENDOTHELIAL CELLS TOWARD SOMATIC GENE THERAPY FOR HEMOPHILIA B

AUTHOR: YAO S-N (Reprint); WILSON J M; NABEL E G; KURACHI S; HACHIYA H L; KURACHI K

AUTHOR ADDRESS: DEP HUMAN GENETICS, UNIV MICHIGAN MED SCH, ANN ARBOR, MICH 48109-0618, USA**USA

JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 88 (18): p8101-8105 1991

ISSN: 0027-8424

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: ENGLISH

...ABSTRACT: and direct contact with the circulating blood, suggest that CECs can serve as an efficient drug delivery vehicle producing factor IX in a somatic gene **therapy** for hemophilia B.

2/3,K/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2006 BIOSIS. All rts. reserv.

0007310757 BIOSIS NO.: 199090095236

EXPRESSION OF HUMAN FACTOR IX IN RABBIT HEPATOCYTES BY RETROVIRUS-MEDIATED GENE TRANSFER POTENTIAL FOR GENE THERAPY OF HEMOPHILIA B

AUTHOR: ARMENTANO D (Reprint); THOMPSON A R; DARLINGTON G; WOO S L C

AUTHOR ADDRESS: HOWARD HUGHES MEDICAL INST, DEP CELL BIOLOGY, BAYLOR COLL MED, HOUSTON, TEXAS 77030, USA**USA

JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 87 (16): p6141-6145 1990

ISSN: 0027-8424

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: ENGLISH

...ABSTRACT: assays. These results establish the feasibility of using infected hepatocytes for the expression of this protein and are a step toward the goal of correcting **hemophila B** by hepatic gene transfer.

?

Set	Items	Description
S1	2	(HEMOPHILA (W) B) (S) (THERAPY OR TREATMENT)
S2	2	RD (unique items)

?

(FACTOR (W) VIII) (S) (VECTOR)
>>>When using accession numbers with KEEP in OneSearch, you
>>>must use the FROM option to specify a file number.

?

S (FACTOR (W) VIII) (S) (VECTOR OR PLASMID)
2511338 FACTOR
87314 VIII
305693 VECTOR
205496 PLASMID
S3 457 (FACTOR (W) VIII) (S) (VECTOR OR PLASMID)

?

S S3 (S) (PULMONARY OR LUNG OR INTRANASAL)
457 S3
1118201 PULMONARY
1137972 LUNG
38141 INTRANASAL
S4 21 S3 (S) (PULMONARY OR LUNG OR INTRANASAL)

?

S S4 AND (HEMOPHILIA (W) B)
21 S4
36686 HEMOPHILIA
2238482 B
6542 HEMOPHILIA(W)B
S5 0 S4 AND (HEMOPHILIA (W) B)

?

RD S4
S6 11 RD S4 (unique items)

?

T S6/3,K/ALL

6/3,K/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

19760175 PMID: 16361563

Overexpression of stefin A in human esophageal squamous cell carcinoma cells inhibits tumor cell growth, angiogenesis, invasion, and metastasis.

Li Wendong; Ding Fang; Zhang Liyong; Liu Zhongmin; Wu Yu; Luo Aiping; Wu Min; Wang Mingrong; Zhan Qimin; Liu Zhihua

National Laboratory of Molecular Oncology, Cancer Institute, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, P.R. China.

Clinical cancer research - an official journal of the American Association for Cancer Research (United States) Dec 15 2005, 11 (24 Pt 1) p8753-62, ISSN 1078-0432--Print Journal Code: 9502500

Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

... cathepsin B activity and inhibited the Matrigel invasion. Overexpression of stefin A delayed the in vitro and in vivo growth of cells and significantly inhibited lung metastasis compared with 50% of lung metastasis in xenograft mice from EC9706 or empty vector cells. Transfection with stefin A showed a dramatic reduction of factor VIII staining in the tumors of xenograft mice. CONCLUSIONS: Our data strongly indicate that stefin A plays an important role in the growth, angiogenesis, invasion, and...

6/3,K/2 (Item 2 from file: 155)
DIALOG(R)File 155: MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

14901673 PMID: 15157331
[In vivo transfection and expression of human coagulant factor VIII cDNA in mice]
Kang Wen-Ying; Wang Hong-Li; Wang Hong; Wang Xue-Feng; Wang Cong-Zhu; Fu Qi-Hua; Ding Qiu-Lan; Wu Wen-Man; Fang Yi; Wang Zhen-Yi
Shanghai Institute of Hematology, Ruijin Hospital, The Shanghai Second Medical University, Shanghai 200025, China.
Zhongguo shi yan xue ye xue za zhi / Zhongguo bing li sheng li xue hui = Journal of experimental hematology / Chinese Association of Pathophysiology (China) Apr 2004, 12 (2) p188-93, ISSN 1009-2137--Print
Journal Code: 101084424
Publishing Model Print
Document type: Journal Article ; English Abstract
Languages: CHINESE
Main Citation Owner: NLM
Record type: MEDLINE; Completed

The aim is to observe the expression of human factor VIII gene in mice transduced in vivo and ex vivo. The vector pLNC-FVIII BD was generated by cloning a B-domain-deleted (760aa-1639aa) FVIII cDNA (FVIIIBD cDNA) into retroviral vector pLNCX. 2 x 10(6) of mouse bone marrow stroma cells transduced by LNC-FVIII BD were infused into 4-week-old BALB/c mice...

...1 contained 15 micro g/mouse) and sacrificed at days 1, 2, 7, 14, 21 and 28, respectively after injection. Tissue such as liver, spleen, lung and kidney were harvested, with which the transcription were detected by means of RT-PCR. In addition, blood was collected to be measured human FVIII...

... inhibitors was not revealed all the time. Syngene image scanning demonstrated that the transcription of the human FVIII BD cDNA occurred mainly in spleen and lung , and secondarily in liver and kidney. No side effects of PAMAM-pLNC-FVIII BD were observed in mice tissue by pathological examination at 4 weeks...

6/3,K/3 (Item 3 from file: 155)
DIALOG(R)File 155: MEDLINE(R)

(c) format only 2006 Dialog. All rts. reserv.

14495641 PMID: 12714372

Lung overexpression of angiostatin aggravates pulmonary hypertension in chronically hypoxic mice.

Pascaud Marie-Aude; Griscelli Frank; Raoul William; Marcos Elisabeth; Opolon Paule; Raffestin Bernadette; Perricaudet Michael; Adnot Serge; Eddahibi Saadia

INSERM U492, Faculte de Medecine, 8 Rue du General Sarrail, 94010 Creteil, France. eddahibi@im3.inserm.fr

American journal of respiratory cell and molecular biology (United States) Oct 2003, 29 (4) p449-57, ISSN 1044-1549--Print Journal Code: 8917225

Publishing Model Print-Electronic

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

... 2.4 versus 30.2 +/- 1.4, respectively), aggravation of right ventricular hypertrophy ($P < 0.05$), and muscularization of distal vessels ($P < 0.01$). Lung **factor VIII**, CD31 immunostaining, as well as eNOS expression were significantly increased after exposure to hypoxia in Ad.CO1-pretreated controls, but decreased in both normoxic and hypoxic animals after treatment with Ad.K3. The results show that inhibition of hypoxia-induced stimulation of lung angiogenic processes aggravates development of hypoxic PH. This suggests that endogenous lung angiogenesis counteracts development of hypoxic PH.

6/3,K/4 (Item 4 from file: 155)

DIALOG(R)File 155: MEDLINE(R)

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13749347 PMID: 12015067

[Preliminary experimental research on gene therapy for hemophilia A]

Yin Jun; Wang Hongli; Hu Yiqun; Wang Xuefeng; Qu Bin; Chu Haiyan; Duan Baohua; Kang Wenyi; Qi Zhengwu; Wang Zhenyi
Shanghai Institute of Hematology, Ruijin Hospital, Shanghai Second Medical University, Shanghai 200025, China.

Zhonghua xue ye xue za zhi = Zhonghua xueyexue zazhi (China) Mar 2002,

23 (3) p138-42, ISSN 0253-2727--Print Journal Code: 8212398

Publishing Model Print

Document type: Journal Article ; English Abstract

Languages: CHINESE

Main Citation Owner: NLM

Record type: MEDLINE; Completed

... expression of human factor VIII (hF VIII) in vivo. METHODS: Human clotting factor VIII cDNA with B-domain deleted (Delta760aa approximately 1639aa) was inserted into **vector** pRC/RSV to form pRC/RSV-hF VIII BD, which conjugated with in vivo liposome transfection reagent (DOTAP-Cholesterol) to accomplish a kind of therapeutic...

... i.m. and sacrificed 48 hours, 10 days, 20 days, 30 days, 40 days and 50 days later, respectively. Tissues such as heart, liver, spleen, lung, kidney and muscle were harvested, the distribution and transcription as well as expression of hF VIII BD cDNA were detected by means of PCR, RT...

6/3,K/5 (Item 5 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

(c) format only 2006 Dialog. All rts. reserv.

12472710 PMID: 10418799

The gene expression of coagulation factor VIII in mammalian cell lines.

Chen C; Fang X D; Zhu J; Wu X F; Zhang Z C; Gu J X; Wang Z Y; Chi C W
Shanghai Institute of Biochemistry, Academia Sinica, China.

Thrombosis research (UNITED STATES) Jul 15 1999, 95 (2) p105-15,
ISSN 0049-3848--Print Journal Code: 0326377

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

... is specific for cells from different tissues. The highest expression level was found in the hepatocellular carcinoma line SMMC-7721, followed by kidney, ovary, and lung cell lines. To compare the efficiency of gene expression of recombinant factor VIII, the factor VIII-deltaB gene was further reconstructed in different forms in the expression plasmid pCMV-dhfr for transient gene expression in Chinese hamster ovary cells. The redundant 5'- and 3'-untranslated sequences of factor VIII-deltaB were deleted. The cDNA encoding the heavy and light chains of factor VIII were constructed, respectively. Among them the high yield of the recombinant factor VIII was found in the coexpression of the heavy and light chain cDNA fragments of factor VIII. The deletion of the redundant 5'-untranslated sequence of factor VIII-deltaB was also beneficial for gene expression. As expected, the gene coexpression of factor VIII-deltaB and von Willibrand Factor cloned by the long-polymerase chain reaction method was also helpful for enhancing the expression level of recombinant factor VIII. A monoclonal antibody raised against factor VIII was prepared and used for the specific assay of recombinant factor VIII by the competitive ELISA method, the assay results were consistent with those determined by the one-stage bioassay.

6/3,K/6 (Item 6 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

(c) format only 2006 Dialog. All rts. reserv.

11533784 PMID: 9367354

Development of immortalized human cerebromicrovascular endothelial cell line as an in vitro model of the human blood-brain barrier.

Muruganandam A; Herx L M; Monette R; Durkin J P; Stanimirovic D B
Cellular Neurobiology Group, Institute of Biological Sciences, National Research Council of Canada, Ottawa, Ontario.

FASEB journal - official publication of the Federation of American Societies for Experimental Biology (UNITED STATES) Nov 1997, 11 (13) p1187-97, ISSN 0892-6638--Print Journal Code: 8804484

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

... specific enzymes alkaline phosphatase and gamma-glutamyl transpeptidase. The diffusion of radiolabeled sucrose across SV-HCEC monolayers was fivefold lower than that observed with human lung microvascular endothelial cells. Furthermore, media conditioned by fetal

human astrocytes increased the transendothelial electrical resistance of SV-HCEC monolayers by 2.5-fold. Therefore, this...

6/3,K/7 (Item 7 from file: 155)
DIALOG(R)File 155: MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

11380850 PMID: 9264782
[Genetic therapy for hemophiliacs--therapeutic potential and technological limits]
Therapie genique des hemophilie--potentialites therapeutiques et limitations technologiques.
Michou A I; Christ M; Pavirani A; Mehtali M
Transgene S.A., Strasbourg, France.
Transfusion clinique et biologique - journal de la Societe francaise de transfusion sanguine (FRANCE) 1997, 4 (3) p251-61, ISSN 1246-7820--
Print Journal Code: 9423846
Publishing Model Print
Document type: Journal Article; Review ; English Abstract
Languages: FRENCH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

... transfer protocol for haemophilia B, we constructed and tested in vitro and in vivo various recombinant adenovirus vectors expressing human FIX. Intravenous administration of this **vector** into various strains of immunocompetent and immunodeficient mice led to an efficient hFIX gene transfer in liver and lung . As a consequence, the hFIX protein was correctly produced and secreted at high levels in the blood of the treated animals. However, expression was transient...

6/3,K/8 (Item 8 from file: 155)
DIALOG(R)File 155: MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

11229023 PMID: 9816156
Interleukin 10 suppresses tumor growth and metastasis of human melanoma cells: potential inhibition of angiogenesis.
Huang S; Xie K; Bucana C D; Ullrich S E; Bar-Eli M
Departments of Cell Biology and Immunology, The University of Texas Anderson Cancer Center, Houston, Texas 77030, USA.
Clinical cancer research - an official journal of the American Association for Cancer Research (UNITED STATES) Dec 1996, 2 (12) p1969-79, ISSN 1078-0432--Print Journal Code: 9502500
Contract/Grant No.: AR 40824; AR; NIAMS; CA 41525; CA; NCI
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

... c. injection into nude mice. The suppression of tumor growth and metastasis was directly correlated with a decrease in neovascularity determined by immunostaining with anti- **factor VIII** . Because tumor-associated macrophages are the major source of angiogenic molecules in melanoma, we used reverse transcription-PCR to demonstrate that IL-10 down-regulates...

6/3,K/9 (Item 9 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

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09624416 PMID: 7683277

Immortalization of epithelial-like cells from human liver tissue with SV40 T-antigen gene.

Miyazaki M; Miura K; Bai L; Kano Y; Tsuboi S; Endo A; Seshimo K; Yoshioka T; Namba M

Department of Cell Biology, Okayama University Medical School, Japan.

Experimental cell research (UNITED STATES) May 1993, 206 (1) p27-35,
ISSN 0014-4827--Print Journal Code: 0373226

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

... were sensitive to cytotoxicity of aflatoxin B1, 3-amino-1,4-dimethyl-5H-pyrido[4,3-b]indole, and benzo[a]pyrene, whereas human embryo lung fibroblasts were insensitive to the cytotoxicity of these carcinogens. These findings suggest that OUMS-21 and -22 cells may arise from undifferentiated liver stem cells...

6/3,K/10 (Item 1 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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0010232509 BIOSIS NO.: 199698700342

Construction of metallothionein-I promoter inserted human blood coagulation factor VIII expression vector and the induction of factor VIII protein synthesis in mouse

AUTHOR: Oh Sang-Hwan (Reprint); Kim Seok-Hyun; Min Yoo-Hong; Kim Young-Soo; Kim Yoon-Soo

AUTHOR ADDRESS: Dep. Biochem. Mol. Biol., Inst. Genetic Sci., Yonsei Univ. Coll. Med., Seoul 120-752, South Korea**South Korea

JOURNAL: Korean Journal of Biochemistry 27 (4): p199-208 1995 1995

ISSN: 0378-8512

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

...ABSTRACT: a recombinant human blood coagulation factor VIII (FVIII) has been attempted by the construction of a mouse metallothionein-I (MT-I) promoter driven eukaryotic expression **vector** system, in order to test the metal-regulated synthesis of FVIII in vivo. For the construction of the MT-I promoter directed FVIII expression **vector** (pMTVIII-B), MT-I promoter sequence was substituted with CMV early promoter in pCMV **vector** and B-domain deleted FVIII cDNA sequence was inserted to the downstream of MT-I promoter. pMTVIII-B was cotransfected with pRSVneo into Chinese hamster...

...pMTVIII-B. Administration of Zn (1 mg/30 g body weight) to mice transfused with pMTVIII-B increased FVIII-B expression in liver, spleen and lung of mice, and the presence of FVIII in the liver of mice was confirmed by immunohistochemical staining. These results suggest that MT-I promoter driven FVIII-B expression **vector** system may be useful for the synthesis and secretion of biologically active recombinant FVIII in

vivo.

6/3,K/11 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE
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06909878 EMBASE No: 1997194320

Gene therapy for hemophiliacs - Therapeutic possibilities and
technological limits
THERAPIE GENIQUE DES HEMOPHILIES - POTENTIALITES THERAPEUTIQUES ET
LIMITATIONS TECHNOLOGIQUES

Michou A.I.; Christ M.; Pavirani A.; Mehtali M.
M. Mehtali, Transgene S.A., 11 Rue de Molsheim, 67000 Strasbourg France
Transfusion Clinique et Biologique (TRANSFUS. CLIN. BIOL.) (France)
1997, 4/3 (251-261)
CODEN: TCBIF ISSN: 1246-7820
DOCUMENT TYPE: Journal; Conference Paper
LANGUAGE: FRENCH SUMMARY LANGUAGE: FRENCH; ENGLISH
NUMBER OF REFERENCES: 25

Defects in the genes encoding the human coagulation factor VIII
(hFVIII) and IX (hFIX) result in life-threatening haemorrhages and severe
arthropathies. While haemophiliacs are currently treated by blood-derived
factors or recombinant hFVIII and...

...transfer protocol for haemophilia B, we constructed and tested in vitro
and in vivo various recombinant adenovirus vectors expressing human FIX.
Intravenous administration of this vector into various strains of
immunocompetent and immunodeficient mice led to an efficient hFIX gene
transfer in liver and lung. As a consequence, the hFIX protein was
correctly produced and secreted at high levels in the blood of the treated
animals. However, expression was transient...
?

Set	Items	Description
S1	2	(HEMOPHILA (W) B) (S) (THERAPY OR TREATMENT)
S2	2	RD (unique items)
S3	457	(FACTOR (W) VIII) (S) (VECTOR OR PLASMID)
S4	21	S3 (S) (PULMONARY OR LUNG OR INTRANASAL)
S5	0	S4 AND (HEMOPHILIA (W) B)
S6	11	RD S4 (unique items)
?		

S S3 AND (HEMOPHILIA (W) B)
457 S3
36686 HEMOPHILIA
2238482 B
6542 HEMOPHILIA(W)B
S7 30 S3 AND (HEMOPHILIA (W) B)
?

S S7 AND (PULMONARY OR LUNG OR INTRANASAL)
30 S7
1118201 PULMONARY
1137972 LUNG
38141 INTRANASAL
S8 0 S7 AND (PULMONARY OR LUNG OR INTRANASAL)
?

Set	Items	Description
S1	2	(HEMOPHILA (W) B) (S) (THERAPY OR TREATMENT)
S2	2	RD (unique items)
S3	457	(FACTOR (W) VIII) (S) (VECTOR OR PLASMID)
S4	21	S3 (S) (PULMONARY OR LUNG OR INTRANASAL)
S5	0	S4 AND (HEMOPHILIA (W) B)
S6	11	RD S4 (unique items)
S7	30	S3 AND (HEMOPHILIA (W) B)
S8	0	S7 AND (PULMONARY OR LUNG OR INTRANASAL)
?		

RD S7
S9 19 RD S7 (unique items)
?

S S9 NOT S6
19 S9
11 S6
S10 19 S9 NOT S6
?

T S10/3,K/ALL

10/3,K/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

15574896 PMID: 16096011

A novel gene expression system: non-viral gene transfer for hemophilia as model systems.

Miao Carol H

Department of Pediatrics, University of Washington and Children's Hospital and Regional Medical Center, Seattle, Washington 98195, USA.

Advances in genetics (United States) 2005, 54 p143-77, ISSN 0065-2660--Print Journal Code: 0370421

Contract/Grant No.: HL69409-02; HL; NHLBI

Publishing Model Print

Document type: Journal Article; Review

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

... integrating vectors. Using in vivo screening of vectors incorporating many different combinations of gene regulatory sequences, liver-specific, high-expressing vectors to accommodate factor IX, factor VIII, and other genes for effective gene transfer have been established. Persistent and high levels of factor IX and factor VIII gene expression for treating hemophilia B and A, respectively, were achieved in mouse livers using hydrodynamics-based gene transfer of naked plasmid DNA incorporating these novel gene expression systems. Some other systems to prolong or stabilize the gene expression following gene transfer are also discussed.

10/3,K/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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15514588 PMID: 15975012

AAV-mediated gene transfer for treatment of hemophilia.

Wang Lixin; Herzog Roland W
Dept. Pediatrics, University of Pennsylvania Medical Center, The Children's Hospital of Philadelphia, Philadelphia, PA 19104, USA.

Current gene therapy (Netherlands) Jun 2005, 5 (3) p349-60, ISSN 1566-5232--Print Journal Code: 101125446

Publishing Model Print

Document type: Journal Article; Review

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

...of two Phase I/II clinical trials to evaluate the safety of AAV-factor IX gene transfer to muscle and liver of patients with severe **hemophilia B**.

Herein, we have reviewed results from studies in animals with hemophilia, early experience with the **vector** system in the clinic, recent innovative approaches in **vector** design and delivery, and strategies to circumvent immunological limitations. Taken together, these studies provide much encouragement for the possibility of future clinical success, but also

...

10/3,K/3 (Item 3 from file: 155)

DIALOG(R)File 155: MEDLINE(R)

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15143362 PMID: 15508114

Gene therapy of the hemophilias.

Lozier Jay
Food and Drug Administration Center for Biologics Evaluation and Research, Rockville, MD 20852-1448, USA. lozier@cber.fda.gov
Seminars in hematology (United States) Oct 2004, 41 (4) p287-96,
ISSN 0037-1963--Print Journal Code: 0404514

Publishing Model Print

Document type: Journal Article; Review

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

... dogs) more closely replicate the requirements for correction of human hemophilia than do mice. Small animals are more convenient to maintain and require significantly less **vector** for testing than do large animals. Nonhemophilic animals (mice or nonhuman primates), whose endogenous **factor VIII** and factor IX complicate analysis of the human proteins, have utility for safety testing of vectors; some assays can discriminate between human coagulation factors and the endogenous coagulation factors. Most animal models suffer the limitations imposed by the immune response to human **factor VIII** or IX protein. Clinical trials have failed to achieve significant **factor VIII** expression in hemophilia A patients, while one clinical trial in **hemophilia B** patients showed only transient therapeutic increments of factor IX expression. Gene therapy remains an investigational method with many obstacles to overcome before it can be...

Descriptors: *Gene Therapy--methods--MT; **Hemophilia B** --therapy--TH

10/3,K/4 (Item 4 from file: 155)

DIALOG(R)File 155: MEDLINE(R)

(c) format only 2006 Dialog. All rts. reserv.

14817480 PMID: 15057309

Novel therapeutic approach for hemophilia using gene delivery of an engineered secreted activated Factor VII.

Margaritis Paris; Arruda Valder R; Aljamali Majed; Camire Rodney M; Schlachterman Alexander; High Katherine A

Division of Hematology, The Children's Hospital of Philadelphia, Abramson Research Center, Philadelphia, Pennsylvania 19104, USA.

Journal of clinical investigation (United States) Apr 2004, 113 (7)

p1025-31, ISSN 0021-9738--Print Journal Code: 7802877

Contract/Grant No.: K01-060580; PHS; U01-HL66948; HL; NHLBI

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

...However, its high cost and short half-life have limited its use. Here, we report a novel treatment strategy with a recombinant adeno-associated virus **vector** delivering a modified FVII transgene that can be intracellularly processed and secreted as activated FVII (FVIIa). We show long-term expression, as well as phenotypic correction of **hemophilia B** mice following gene transfer of the murine FVIIa homolog, with no evidence of thrombotic complications at these doses. These data hold promise for a potential...

; Animals; Factor VIIa--metabolism--ME; **Hemophilia B** --therapy--TH; Humans; Mice; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, P.H.S.; Time Factors

10/3,K/5 (Item 5 from file: 155)

DIALOG(R)File 155: MEDLINE(R)

(c) format only 2006 Dialog. All rts. reserv.

14327287 PMID: 12776156

Gene therapy progress and prospects: gene therapy for the hemophilias.

Walsh Christopher E

Mt Sinai School of Medicine, One Gustave Levy Place, Rm 24-42C Annenberg Building, New York City, NY 10029, USA.

Gene therapy (England) Jun 2003, 10 (12) p999-1003, ISSN 0969-7128
--Print Journal Code: 9421525

Publishing Model Print

Document type: Journal Article; Review

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

... for hemophilia gene transfer require the long-term therapeutic production of the coagulant protein without stimulating an immune response to the transgene product or the **vector**. Based on a scientific understanding of the molecular and cellular defects, leading to the bleeding phenotype, impressive strides have been made in the last 2...

Descriptors: *Gene Therapy--methods--MT; *Hemophilia A--therapy--TH; *
Hemophilia B --therapy--TH

10/3,K/6 (Item 6 from file: 155)

DIALOG(R)File 155: MEDLINE(R)

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14085436 PMID: 12544490

AAV-mediated gene transfer for hemophilia.

High Katherine

University of Pennsylvania School of Medicine, Children's Hospital of Philadelphia, 19104, USA.

Genetics in medicine - official journal of the American College of Medical Genetics (United States) Nov-Dec 2002, 4 (6 Suppl) p56S-61S, ISSN 1098-3600--Print Journal Code: 9815831

Contract/Grant No.: P01 HL64190; HL; NHLBI; R01 HL61921; HL; NHLBI; U01 HL66948; HL; NHLBI

Publishing Model Print

Document type: Journal Article; Review

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

... method of treating hemophilia, an inherited bleeding disorder that results from the absence of functional factor VIII or factor IX. Using an adeno-associated viral **vector** derived from AAV serotype 2, we have shown in mice and in hemophilic dogs that we can achieve long-term expression (>3 years) of clotting...

... skeletal muscle results in factor levels of only 1% to 2%. Based on these results, a trial of AAV-mediated liver-directed gene transfer for **hemophilia B** has been proposed and is reviewed here.

10/3,K/7 (Item 7 from file: 155)

DIALOG(R)File 155: MEDLINE(R)

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14039997 PMID: 12463593

Adeno-associated virus-mediated gene transfer for hemophilia B

High Katherine A

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International journal of hematology (Ireland) Nov 2002, 76 (4) p310-8, ISSN 0925-5710--Print Journal Code: 9111627

Publishing Model Print

Document type: Journal Article; Review

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Adeno-associated virus-mediated gene transfer for hemophilia B

Hemophilia is the bleeding diathesis caused by mutations in the gene encoding factor VIII (hemophilia A) or factor IX (**hemophilia B**). Currently, the disease is treated by intravenous infusion of the missing purified clotting factor. The goal of gene transfer for treating hemophilia is to achieve...

... of AAV. In a staged approach, AAV-factor IX (AAV-F.IX) was first administered at doses of up to 1.8×10^{12} **vector** genomes/kg (vg/kg) into the skeletal muscles of men with **hemophilia B**. This trial established the safety of parenteral administration and also showed that general characteristics of AAV transduction were similar in mice, dogs, and humans. In an ongoing trial, AAV-F.IX is being administered into the hepatic circulation of men with severe **hemophilia B**. The goal of these studies is to identify a safe dose that reliably yields circulating levels of factor IX >2% of normal levels in all subjects. This goal has already been achieved in the **hemophilia B** dog model; the ongoing study will determine whether a similar result can be achieved in humans with

hemophilia B .

Descriptors: *Gene Transfer Techniques; **Hemophilia B --therapy--TH**

10/3,K/8 (Item 8 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

(c) format only 2006 Dialog. All rts. reserv.

13583637 PMID: 12174674

Gene therapy for hereditary hematological disorders.

Herzog R W; Hagstrom J N

Department of Pediatrics, Children's Hospital of Philadelphia, University of Pennsylvania Medical Center, Philadelphia, Pennsylvania, USA.
rwherzog@mail.med.upenn.edu

American journal of pharmacogenomics - genomics-related research in drug development and clinical practice (New Zealand) 2001, 1 (2) p137-44,
ISSN 1175-2203--Print Journal Code: 100967746

Publishing Model Print

Document type: Journal Article; Review

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

... utilizing either an ex vivo, non-viral gene transfer technique or an intravenous infusion of a retroviral vector to treat adults with severe hemophilia A (**factor VIII** deficiency). The third study involves intramuscular administration of an adeno-associated viral (AAV) **vector** for expression of factor IX in adult patients with **hemophilia B** . Results from this study and from preclinical studies preceding the trial demonstrate that it is possible to safely administer high doses of a viral **vector** in vivo.

10/3,K/9 (Item 9 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

(c) format only 2006 Dialog. All rts. reserv.

13581720 PMID: 12109144

Viral vector-mediated gene therapy for hemophilia.

VandenDriessche T; Collen D; Chuah M K

Center for Transgene, Technology and Gene Therapy, Flanders Interuniversity Institute for Biotechnology, University of Leuven, 49 Herestraat B-3000 Leuven, Belgium. thierry.vandendriessche@med.kuleuven.ac.be

Current gene therapy (Netherlands) Sep 2001, 1 (3) p301-15, ISSN 1566-5232--Print Journal Code: 101125446

Publishing Model Print

Document type: Journal Article; Review

Languages: ENGLISH

Main Citation Owner: NLM .

Record type: MEDLINE; Completed

...Significant progress has been made recently in the development of gene therapy for hemophilia. This has been primarily due to the technical improvements of existing **vector** systems and the development of new gene delivery methods. Therapeutic and sometimes physiologic levels of FVIII and FIX could be achieved in FVIII- and FIX...

Descriptors: *Gene Therapy; *Genetic Vectors; *Hemophilia A--therapy--TH; * **Hemophilia B --therapy--TH**; Adenoviridae--genetics--GE; Animals; Clinical Trials, Phase I; Dependovirus--genetics--GE; Dogs; Factor IX

--genetics--GE; Factor VIII--genetics--GE; Hemophilia A--genetics--GE;
Hemophilia B--genetics--GE; Humans; Lentivirus--genetics--GE; Mice;
Moloney murine leukemia virus--genetics--GE

10/3,K/10 (Item 10 from file: 155)
DIALOG(R)File 155: MEDLINE(R)
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13148656 PMID: 11269333

Gene therapy for hemophilia.

Chuah M K; Collen D; VandenDriessche T
Center for Transgene Technology and Gene Therapy, Flanders
Interuniversity Institute for Biotechnology, University of Leuven, Belgium.
journal of gene medicine (England) Jan-Feb 2001, 3 (1) p3-20, ISSN
1099-498X--Print Journal Code: 9815764
Publishing Model Print
Document type: Journal Article; Review
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

... recently been made in the development of gene therapy for the treatment of hemophilia A and B. These advances parallel the technical improvements of existing **vector** systems including MoMLV-based retroviral, adenoviral and AAV vectors, and the development of new delivery methods such as lentiviral vectors, helper-dependent adenoviral vectors and...

... are currently ongoing in patients suffering from severe hemophilia A or B. No significant adverse side-effects were reported, and semen samples were negative for **vector** sequences by sensitive PCR assays. Most importantly, some subjects report fewer bleeding episodes and occasionally have very low levels of clotting factor activity detected. The...

Descriptors: *Gene Therapy; *Hemophilia A--therapy--TH; * **Hemophilia B**--therapy--TH

10/3,K/11 (Item 1 from file: 5)
DIALOG(R)File 5: Biosis Previews(R)
(c) 2006 BIOSIS. All rts. reserv.

0015576654 BIOSIS NO.: 200510271154

A novel deletion in the FVIIIB-domain that reduces transgene size while preserving FVIII activity

AUTHOR: Liu Yi-Lin (Reprint); Zhu Hua; Schlachterman Alexander; Chang Heesoon; Camire Rodney M; High Katherine A
AUTHOR ADDRESS: Childrens Hosp, Philadelphia, PA 19104 USA**USA
JOURNAL: Blood 104 (11, Part 1): p869A NOV 16 2004 2004
CONFERENCE/MEETING: 46th Annual Meeting of the American-Society-of-Hematology San Diego, CA, USA December 04 -07, 2004; 20041204
SPONSOR: Amer Soc Hematol
ISSN: 0006-4971
DOCUMENT TYPE: Meeting; Meeting Poster
RECORD TYPE: Abstract
LANGUAGE: English

...ABSTRACT: good target disease for gene therapy. Adeno-associated virus (AAV) vectors have proven successful for the delivery of the factor IX gene in humans with **hemophilia B**. For the treatment of hemophilia A,

a problem in the packaging of the rFVIII cDNA or various B-domainless derivatives (i.e. rFVIII-SQ) in...

...a 4-8-fold increase in specific activity compared to FVIII-SQ. We further tested whether FVIII-RKR could function in an in vivo setting.

Plasmid DNA (50 mu g) containing FVIII-RKR or FVIII-SQ with liver-specific mouse transthyretin (mTTR) promoter were introduced into hemophilia A (HA) mice hydrodynamically...

...expression cassette of mTTR promoter and FVIII-SQ have been administered. Expression of physiological FVIII levels was observed in high dose group (4.0E+12 **vector** genome per animal, n=4). FVIII activity averages 1.88 U/ml by Coamatic assay or 0.81 U/ml by aPTT assay at 12 weeks post injection. In low dose group (1.0E+12 **vector** genome per animal, n=5) therapeutic level of FVIII is achieved, 0.59 U/ml by Coamatic assay or 0.23 U/ml by aPTT assay...

...and shown to have similar packaging efficiency to AAV-FVIII-SQ. Studies are currently underway with AAV-FVIII-RKR to evaluate the ability of this **vector** to drive long-term expression of functional protein. In summary, we developed a novel FVIII molecule that has high specific activity and is suitable for...

10/3,K/12 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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0013627016 BIOSIS NO.: 200200220527

Long-term expression of activated FVII in vivo following AAV-mediated liver gene transfer: Implications for treatment with continuous infusion of recombinant activated FVII

AUTHOR: Margaritis Paris (Reprint); Arruda Valder R (Reprint); High Katherine A (Reprint)

AUTHOR ADDRESS: Pediatrics, Children's Hospital of Philadelphia, Philadelphia, PA, USA**USA

JOURNAL: Blood 98 (11 Part 1): p696a November 16, 2001 2001

MEDIUM: print

CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001; 20011207

SPONSOR: American Society of Hematology

ISSN: 0006-4971

DOCUMENT TYPE: Meeting; Meeting Abstract; Meeting Poster

RECORD TYPE: Abstract

LANGUAGE: English

...ABSTRACT: be used in a hemophilic mouse model. To further study the long-term effect of continuous FVIIa expression, we constructed a recombinant AAV-2 viral **vector** carrying this FVIIa transgene under the control of a liver-specific promoter and injected **vector** into the portal circulation in hemostatically normal immunodeficient mice (n=7) at doses ranging from 1.5X10¹¹ **vector** genomes (v.g.)/mouse to 2.4X10¹² v.g./mouse. Mouse plasma was collected and assayed for antigen levels by an ELISA specific for human...

DESCRIPTORS:

...DISEASES: **hemophilia B** --

...MESH TERMS: **Hemophilia B** (MeSH)

10/3,K/13 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

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0013627009 BIOSIS NO.: 200200220520

Induction of immunological tolerance to a coagulation factor antigen by hepatic gene transfer

AUTHOR: Migozzi Federico (Reprint); Arruda Valder R (Reprint); Liu Yi-Lin (Reprint); Wang YuQuin (Reprint); Liu Jian Hua (Reprint); Kaufhold Antje (Reprint); High Katherine A (Reprint); Herzog Roland W (Reprint)

AUTHOR ADDRESS: Pediatrics and Pathology, Childrens Hospital of Philadelphia and University of Pennsylvania Medical Center, Philadelphia, PA, USA**USA

JOURNAL: Blood 98 (11 Part 1): p694a November 16, 2001 2001

MEDIUM: print

CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001; 20011207

SPONSOR: American Society of Hematology

ISSN: 0006-4971

DOCUMENT TYPE: Meeting; Meeting Abstract; Meeting Poster

RECORD TYPE: Abstract

LANGUAGE: English

...ABSTRACT: therapy is an attractive alternative to conventional treatment of hemophilia, because efficient and sustained expression of factor VIII (hemophilia A) or factor IX (F.IX, **hemophilia B**) would provide a continuous supply of factor. A potentially serious complication of treatment is the formation of neutralizing antibody (inhibitor) against the coagulation factor. It...

...17 months, experiment ongoing) of canine F.IX (at levels of 5-12% of normal) after adeno-associated virus (AAV)-mediated hepatic gene transfer in **hemophilia B** dogs with a F.IX null mutation. Animals of this strain without exception formed inhibitors in other gene replacement strategies. Here, we demonstrate in murine models that hepatic AAV-F.IX transduction following introduction of **vector** into the portal circulation can induce tolerance to the expressed F.IX antigen. Normal mice of 4 different strains (C57BL/6, BALB/c, C3H, CD-1) received AAV **vector** expressing human F.IX (hF.IX) from the EF1alpha promoter (n=4 per strain, 1-3X10¹¹ **vector** genomes/mouse) by splenic capsule injection. Except for CD-1 mice that formed anti-hF.IX by 4 weeks, mice of all other strains showed...

...hepatocyte-derived expression of the antigen is likely sufficient for tolerance induction. Interestingly, naive mice formed high titer anti-hF.IX after introduction of the **vector** to skeletal muscle indicating that the tolerizing effect of gene transfer is dependent on the target tissue. Anti-hF.IX formation in CD-1 mice...

...observed for the other strains), but mostly Th1-driven after hepatic gene transfer suggesting differences in activation of CD4+ T helper cells in these tissues. **Hemophilia B** mice (BALB/c or C3H background) with no endogenous F.IX expression formed anti-hF.IX after gene transfer, albeit transiently in some animals, but showed sustained expression without anti-F.IX formation when the species-specific murine F.IX transgene was used. This treatment was also successful in **hemophilia B** /CD-1 mice. Since our observations were not limited to a particular strain of mice, AAV-mediated hepatic gene transfer may generally be useful for inducing tolerance to a F.IX antigen. Therefore, these results are encouraging for in vivo administration of AAV vectors to **hemophilia B** patients with severe F.IX mutations, and illustrate the potential of gene transfer as a tool for induction of antigen-specific immune

tolerance.

DESCRIPTORS:

DISEASES: **hemophilia B** --

MESH TERMS: **Hemophilia B** (MeSH)

10/3,K/14 (Item 4 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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0013139633 BIOSIS NO.: 200100311472

In utero delivery of AD-CMV-HFIX results in correction of hemophilia B in the neonatal period

AUTHOR: Lipshutz Gerald S (Reprint); Wang Lili; Gaensler Karin M L (Reprint)

AUTHOR ADDRESS: Medicine and Surgery, University of California, San Francisco, CA, USA**USA

JOURNAL: Blood 96 (11 Part 2): p387b November 16, 2000 2000

MEDIUM: print

CONFERENCE/MEETING: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000; 20001201

SPONSOR: American Society of Hematology

ISSN: 0006-4971

DOCUMENT TYPE: Meeting; Meeting Abstract

RECORD TYPE: Abstract

LANGUAGE: English

In utero delivery of AD-CMV-HFIX results in correction of hemophilia B in the neonatal period

ABSTRACT: **Hemophilia B** affects about 1 in 25,000 males. Severely affected neonates are at increased risk for catastrophic perinatal bleeding. Recent advances in the development of factor...

...likely to occur with vector-derived factor IX expression in adult patients. The development of strategies for the induction of immune tolerance to factor IX, **factor VIII**, and other therapeutic proteins will be important for the future success of gene therapy-based treatments for genetic disorders. In this study, we have assessed whether therapeutic levels of factor IX could be produced in a murine model of **hemophilia B** after injection of a viral gene delivery **vector** prenatally. An adenoviral human factor IX (HFIX) **vector** (Ad-HFIX) was generated by initially subcloning full length HFIX (provided by Darrel W. Stafford, University of North Carolina) between a CMV promoter and SV40 polyadenylation signal. This construct was subcloned into a shuttle **plasmid** before co-transfected 293 cells with a serotype 5, E1- and E3-deleted replication-deficient recombinant adenoviral **plasmid**. **Hemophilia B** carrier female mice (XHX) produced by a targeted disruption of the murine factor IX gene (provided by Inder Verma, Salk Institute) were bred with XHY...

DESCRIPTORS:

...DISEASES: **hemophilia B** --

MESH TERMS: **Hemophilia B** (MeSH)

10/3,K/15 (Item 1 from file: 73)

DIALOG(R)File 73:EMBASE

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12607027 EMBASE No: 2004199158

Preclinical animal models for hemophilia gene therapy: Predictive value and limitations

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Seminars in Thrombosis and Hemostasis (SEMIN. THROMB. HEMOST.) (United States) 2004, 30/2 (205-213)

CODEN: STHMB ISSN: 0094-6176

DOCUMENT TYPE: Journal ; Review

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 57

...design of gene therapy protocols, and over the last 5 years it has been shown that long-term phenotypic correction, with sustained therapeutic levels of **factor VIII** (FVIII) and factor IX (FIX), can be attained in FVIII- and FIX-deficient mice and dogs using various viral **vector**-mediated gene therapy approaches. These animal models also have elucidated potential complications of gene therapy protocols, including acute **vector**-associated toxicities and the induction of neutralizing antibodies to the FVIII and FIX transgene products. Nevertheless, although the preclinical paradigm of hemophilic mouse followed by...

MEDICAL DESCRIPTORS:

disease model; prediction; hemophilia A--drug therapy--dt; **hemophilia B**--drug therapy--dt; somatic cell; phenotype; drug efficacy; drug safety; drug design; virus vector; toxicity; dog; drug screening; gene targeting; gene expression; drug infusion; gene...

10/3,K/16 (Item 2 from file: 73)

DIALOG(R)File 73:EMBASE

(c) 2006 Elsevier Science B.V. All rts. reserv.

12607026 EMBASE No: 2004199157

Nonviral gene therapy approaches to hemophilia

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Seminars in Thrombosis and Hemostasis (SEMIN. THROMB. HEMOST.) (United States) 2004, 30/2 (197-204)

CODEN: STHMB ISSN: 0094-6176

DOCUMENT TYPE: Journal ; Review

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 92

The goal of hemophilia gene therapy is to obtain long-term therapeutic levels of **factor VIII** (FVIII) or factor IX (FIX) without stimulating an immune response against the transgene product or the **vector**. The success of gene therapy is largely dependent on the development of appropriate gene delivery vectors. Both viral vectors and nonviral vectors have been considered...

MEDICAL DESCRIPTORS:

...transgene; gene delivery system; virus vector; drug efficacy; disease model; inflammation; gene expression; risk assessment; carcinogenesis; cancer risk; randomization; phenotype; hemophilia A--drug therapy--dt; **hemophilia B**--drug therapy--dt; drug formulation; genome; gene transfer; liver; electroporation; injection; drug targeting; drug delivery system; target cell; ex vivo study; transposon; gene mutation; human...

10/3,K/17 (Item 3 from file: 73)

DIALOG(R)File 73:EMBASE

(c) 2006 Elsevier Science B.V. All rts. reserv.

12607025 EMBASE No: 2004199156

**Onco-retroviral and lentiviral vector-based gene therapy for hemophilia:
Preclinical studies**

Van Damme A.; Chuah M.K.L.; Collen D.; VandenDriessche T.

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AUTHOR EMAIL: thierry.vandendriessche@med.kuleuven.ac.be

Seminars in Thrombosis and Hemostasis (SEMIN. THROMB. HEMOST.) (United States) 2004, 30/2 (185-195)

CODEN: STHMB ISSN: 0094-6176

DOCUMENT TYPE: Journal ; Review

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 96

Hemophilia A and B gene therapy requires long-term and stable expression of coagulation **factor VIII** (FVIII) or factor IX (FIX), respectively, and would need to compare favorably with protein replacement therapy. Onco-retroviral and lentiviral vectors are attractive vectors for...

...remain a major issue that must be resolved before the full potential of these vectors eventually can be exploited clinically. Nevertheless, the continued progress in **vector** design combined with a better understanding of **vector** biology may ultimately yield more effective gene therapy approaches using these integrating vectors.

MEDICAL DESCRIPTORS:

retrovirus vector; lentivirus vector; hemophilia A--drug therapy--dt;
hemophilia B --drug therapy--dt; protein expression; target cell; genome; genetic transduction; cell type; cell division; ex vivo study; in vivo study; evaluation; gene delivery system; liver...

10/3,K/18 (Item 4 from file: 73)

DIALOG(R)File 73:EMBASE

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12607023 EMBASE No: 2004199154

Preclinical gene therapy studies for hemophilia using Adeno-Associated Virus (AAV) vectors

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Seminars in Thrombosis and Hemostasis (SEMIN. THROMB. HEMOST.) (United States) 2004, 30/2 (161-171)

CODEN: STHMB ISSN: 0094-6176

DOCUMENT TYPE: Journal ; Review

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 57

...IX (FIX), although the levels vary. Intrahepatic delivery is more efficacious than intravenous administration, which is superior to intramuscular delivery. The recent development of efficient **factor VIII** (FVIII) expression cassettes has made AAV-based gene therapy for hemophilia A also within reach. Although no acute toxicity has been observed with any route of administration, an increased risk of antibody formation against

FIX has been noted following intramuscular delivery. Biodistribution studies concluded that the **vector** disseminates to most tissues in a dose-dependent and time-dependent manner, but the majority of the **vector** resides in the targeted tissue. In addition, the risk of germline transmission has been shown to be low or absent. The relatively recent isolation of...

...be addressed. Delivery of AAV to large animals has not been reproducible, which could be due to nonoptimized delivery and/or immune responses to the **vector** or transgene product. In addition, a complete understanding of the biology of these vectors is required to assess their long-term safety. Solving these issues...

MEDICAL DESCRIPTORS:

...safety; disease model; drug efficacy; drug administration route; antibody production; risk assessment; dose time effect relation; virus isolation; serotype; immune response; drug delivery system; transgene; **hemophilia B** --drug therapy--dt; dose response; hemostasis; liver; drug potency; gene expression; peripheral vein; hemophilia A--drug therapy--dt; toxicity; drug tolerability; drug bioavailability; mutagenesis; human...

10/3,K/19 (Item 5 from file: 73)

DIALOG(R)File 73:EMBASE

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11292970 EMBASE No: 2001308599

Gene therapy of hemophilia

Schwaab R.; Oldenburg J.

Dr. R. Schwaab, Inst. Exp. Haematol./Transfus. Med., Sigmund-Freud-Str. 25, 53105 Bonn Germany

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Seminars in Thrombosis and Hemostasis (SEMIN. THROMB. HEMOST.) (United States) 2001, 27/4 (417-424)

CODEN: STHMB ISSN: 0094-6176

DOCUMENT TYPE: Journal ; Review

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 50

Hemophilia A and B are X-linked bleeding disorders caused by mutations within the **factor VIII** and factor IX genes, respectively. Although both disorders can be easily treated by substitution with concentrates of functional **factor VIII** and factor IX, considerable effort has been undertaken to develop a gene therapy for hemophilia in order to improve patients' life quality and reduce high costs of therapy. The principle of gene therapy is the introduction of an intact copy of the **factor VIII** /factor IX gene in somatic cells, compensating for the defective gene. To do this, retroviral, adenoviral, and adeno-associated virus (AAV) **vector** systems, among others, were used. Encouraged by the results of preliminary experiments using preponderant mouse and canine models, three clinical phase I studies on hemophilia...

MEDICAL DESCRIPTORS:

*hemophilia A--disease management--dm; *hemophilia A--drug therapy--dt; *hemophilia A--etiology--et; * **hemophilia B** --disease management--dm; * **hemophilia B** --drug therapy--dt; * **hemophilia B** --etiology--et; *gene therapy
?

Set	Items	Description
S1	2	(HEMOPHILA (W) B) (S) (THERAPY OR TREATMENT)

```
S2      2 RD  (unique items)
S3      457 (FACTOR (W) VIII) (S) (VECTOR OR PLASMID)
S4      21 S3 (S) (PULMONARY OR LUNG OR INTRANASAL)
S5      0 S4 AND (HEMOPHILIA (W) B)
S6      11 RD S4 (unique items)
S7      30 S3 AND (HEMOPHILIA (W) B)
S8      0 S7 AND (PULMONARY OR LUNG OR INTRANASAL)
S9      19 RD S7 (unique items)
S10     19 S9 NOT S6
?
```

COST

```
04apr06 15:40:16 User259876 Session D859.2
$3.04    0.894 DialUnits File155
$4.18    19 Type(s) in Format 3
$4.18    19 Types
$7.22   Estimated cost File155
$5.57    0.945 DialUnits File5
$1.12    7 Type(s) in Format 95 (KWIC)
$1.12    7 Types
$6.69   Estimated cost File5
$8.97    0.801 DialUnits File73
$18.60   6 Type(s) in Format 3
$18.60   6 Types
$27.57   Estimated cost File73
OneSearch, 3 files, 2.640 DialUnits FileOS
$3.46    INTERNET
$44.94   Estimated cost this search
$45.81   Estimated total session cost 2.873 DialUnits
?
```

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